Paper No. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte KENJI FUKUDOME and CHARLES T. ESMON

Appeal No. 2004-1213
Application No. 09/378,261

ON BRIEF

ELLIS, SCHEINER and MILLS, Administrative Patent Judges.

ELLIS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 16, 17 and 27-30, all the claims pending in the application. Claims 1-15 and 18-23 have been canceled. Claims 24-26 are objected to but, according to the examiner,

would be allowable if re-written in an independent form.[1] Paper No. 13, p. 4.

Claims 16, 17, 27 and 28 are illustrative of the subject matter on appeal and read as follows:

> 16. A method for enhancing an inflammatory response involving blocking of protein C or activated protein C binding to an endothelial cell protein C/activated protein C receptor comprising administering to a patent in need of treatment thereof an amount of a compound blocking binding of protein C or activated protein C to the receptor by binding to the endothelial cell protein C/activated protein C receptor.
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> 17. The method of claim 16 wherein the compound is selected from the group consisting of antibodies and fragments of antibodies to the receptor, nucleic acid sequences inhibiting expression of the receptor, and synthetic or natural compounds other than protein peptides or nucleic acid sequences which inhibit binding.
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> 27. The method of claim 16 wherein the compound is an oligonucleotide
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> 28. The method of claim 16 wherein the compound is a receptor fragment.

The examiner has not relied on any references in rejecting the claims.

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[1] We note the appellants' statement on page 2 of the Substitute Appeal Brief (hereinafter, Brief) that a "proposed amendment rewriting claim 24 in independent form accompanies this brief." We point out that claim 24 is not under rejection and, therefore, is not before us.

In addition, attention is directed to 37 C.F.R. § 1.195(2003)(now, 37 C.F.R. § 41.41(a)(2)) which states that after appeal any new evidence "will not be admitted without a showing of good and sufficient reasons why they were not earlier presented." See also, 37 C.F.R. § 116(a)(2003), now § 41.41(b). The appellants are herein advised that the amended claim has not been entered into the file.

The claims stand rejected as follows:

I. Claims 16, 17 and 27-30 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

II. Claims 16, 17 and 27-30 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

We have considered the respective positions of both the appellants and the examiner and find ourselves in substantial agreement with that of the examiner. Accordingly, we affirm.

Background

Blood coagulation is a process by which the body prevents blood loss by forming a blood clot. Protein C is an essential component in the blood coagulation process. Specification, p. 1, lines 6-7. Protein C is made in the liver and circulates in the blood in an inactive form. It is converted to its active form with the help of thrombin bound to thrombomodulin. Id., lines 30-32. Activated protein C, in combination with protein S,

degrades factors VIIIa and Va thereby limiting the activity of these factors in the coagulation cascade. The results of several studies involving protein C suggest that it may control coagulation and influence inflammation. Id., lines 20-22.

The specification discloses the cloning and characterization of an endothelial cell protein C binding protein receptor (EPCR). The EPCR is said to bind both protein C and activated protein C. Specification, p. 3, lines 15-18. According to the specification, both EPCR mRNA production and binding function are down-regulated by cytokines such as TNF (tumor necrosis factor). Id., lines 18-20. The results of assays using TNF are said to show that the EPCR "is subject to regulation by inflammatory cytokines, and can therefore be used to modulate inflammatory responses in which protein C or activated protein C (APC) is involved." Id., lines, 21-26.

The present invention is said to be useful in the enhancement of inflammatory responses by blocking protein C or activated protein C binding to the EPCR present in endothelial cells with a compound capable of binding to said EPCR. Specification, p. 18, lines 23-26. Compounds which are effective in blocking binding of the EPCR are said to include antibodies to the EPCR, fragments of antibodies, oligonucleotides, synthetic compounds, receptor fragments, etc.

Discussion

The examiner argues that the specification fails to provide an adequate written description of the subject matter recited in the claims. Answer, p. 5.

With respect to claim 16, the examiner argues that the specification discloses methods of using antibodies, and parts thereof, to block the binding of protein C and activated protein C (APC) to the EPCR, but that it does not provide an adequate written description of the binding of other compounds to said receptor. Answer, p. 5. For example, the examiner points out that the specification fails to describe any receptor fragments that can bind to the receptor itself as set forth in dependent claim 28. Id., p. 6.

With respect to claim 17, the examiner argues that on pages 25-27, the specification alludes to other compounds which may bind to the EPCR, however, it fails to provide an adequate written description of, or even name, any "synthetic or natural compounds other than proteins, peptides or nucleic acid sequences which inhibit binding" of protein C and APC to the EPCR. Answer, p. 7.

With respect to claim 27, the examiner points out that antisense oligonucleotides can be designed which (i) are complementary to a nucleotide sequence; and (ii) inhibit the expression of the protein product encoded by said sequence. Answer, p. 6. An antisense oligonucleotide acts by binding to a target nucleotide sequence and preventing translation of the protein which said sequence encodes. The examiner

further points out that the specification discloses that antisense oligonucleotides can be designed which inhibit the production of new EPCR thereby decreasing the number of receptors produced by a cell. Id., pp. 6-7. However, the examiner argues that the specification does not describe any oligonucleotides which bind to the EPCR and block binding of protein C or APC as required by claim 27. Id., p. 7.

In response, the appellants contend that claims 16, 29 and 30 do not recite oligonucleotides or receptor fragments. Brief, p. 14 and 15. According to the appellants, support for the subject matter of claim 16 can be found in the section of the specification which describes the generation of antibodies for diagnostic or therapeutic use, and in claim 16 as originally filed. Id. The appellants argue that the examiner has not made any rejection with respect to the pharmaceutical carrier recited in claim 29. Id., p. 15.

With respect to claims 17, 27 and 28, the appellants argue that the specification discloses methods for preparing receptor fragments as well as the full amino acid sequence of the EPCR. Brief, p. 14. The appellants further argue that the specification also discloses methods of making oligonucleotides as well as the complete nucleotide sequence of the APC receptor. Id.

We find the appellants' arguments unpersuasive.

It is well established that to satisfy the written description requirement, the inventor "must convey with reasonable clarity to those skilled in the art that, as of the

filing date sought, he or she was in possession of the invention" [emphasis added]. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

We recognize that it is not necessary for the specification to describe the claimed invention ipsissimis verbis; all that is required is that it reasonably convey to those skilled in the art that, as of the filing date sought, the inventor was in possession of the claimed invention. Union Oil of California v. Atlantic Richfield Co., 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000); Vas-Cath Inc. v. Mahurkar, 935 F.2d at 1563-64, 19 USPQ2d at 1119; In re Gosteli, 872 F.2d 1008,1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989); In re Edwards, 568 F.2d 1349, 1351-52,196 USPQ 465, 467 (CCPA 1978). However, the specification must describe the invention in sufficient detail that one skilled in the art can recognize that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

We note that all the claims in the present application are directed to a method. To that end, we point out that our appellate reviewing court has held that when it comes to providing an adequate written description of the invention, the standard is the same. As stated by the court in University of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926, 69 USPQ2d 1886, 1894 (Fed. Cir. 2004):

> "[r]egardless of whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.

Here, we find that one skilled in the art cannot practice the claimed method of an enhancing an inflammatory response without being in possession of a compound which is capable of binding to the EPCR. We further find that claim 16 is a genus claim directed to the use of any compound capable of binding to the referenced receptor. The dependent claims indicate that said genus encompasses several subgenera, such as natural and synthetic compounds (claim 17), oligonucleotides (claim 27) and receptor fragments (claim 28), wherein the species in said subgenera are capable, inter alia, of binding the EPCR .

Over the past decade, the Federal Circuit has considered several cases with respect to what a specification must disclose in order to provide an adequate written description of a DNA sequence. See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002); University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1406 (Fed. Cir. 1997); Fiers v. Revel, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993). To that end, the court has held that for a DNA sequence, an adequate written description "requires a precise definition, such as by structure, formula, [or] chemical name sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d at 1566, 43 USPQ2d at 1405,

quoting, Fiers v. Revel, 984 F.2d at 1171, 25 USPQ2d at 1606 (written description of a DNA is usually achieved by reciting the nucleotide sequence of which it consists). Nevertheless, the court has suggested that a functional definition of a compound, including DNA, may be sufficient for purposes of written description provided there is a "structure-function relationship known to those of ordinary skill in the art." In re Wallach, 378 F.3d 1330, 71 USPQ2d 1939, 1943 (Fed. Cir. 2004); see also, University of Rochester v. G.D. Searle & Co., 358 F.3d 916, 925, 69 USPQ2d 1886, 1893 (Fed. Cir. 2004); Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1327, 63 USPQ2d 1609, 1615 (Fed. Cir. 2002).

Here, we find that the compounds required to practice the methods set forth in the generic and subgeneric claims are described strictly by their function; i.e., any compound which binds to an endothelial cell protein C or activated protein C receptor in a manner which blocks binding of protein C or activated protein C to said receptor.

Turning first to claim 16, we agree with the examiner that the disclosure of an antibody does not provide an adequate written description of the genus of compounds set forth therein. We find that the disclosure of a single species (i.e., the antibody), having the claimed functional characteristics does not begin to describe the structure of the numerous and disparate compounds encompassed by the claim, which includes compounds having a multitude of different structures; e.g., oligonucleotides, receptor fragments, etc. The description of an antibody does not define any structural features

commonly possessed by members of the genus. Nor is there a correlation between the structure of an antibody molecule and the structure other compounds having the same function. We further find that the structure of other compounds capable of binding the EPCR in a manner which blocks binding of protein C or activated protein C cannot be deduced from the structure an antibody. Therefore, one skilled in the art cannot visualize or recognize the identify of other members of the genus from the description of an antibody. Accordingly, we find that the specification does not reasonably convey to those skilled in the art that the appellants were in possession of the genus (of compounds) having the claimed functional properties and, therefore, it does not convey that they were in possession of the method set forth in claim 16. Vas-Cath Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116. See also, University of California v. Eli Lilly and Co., 119 F.3d at 1559, 43 USPQ2d at 1406("A definition by function, ... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is"); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)(determining that the disclosure of two chemical compounds within a subgenus did not describe that subgenus); In re Grimme, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960)("[I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. . . . However it may not be necessary to enumerate a plurality of species if a

genus is sufficiently identified in an application by 'other appropriate language'"); In re Smythe, 480, F.2d 1376, 1383,178 USPQ 279, 284 (CCPA 1973).

With respect to the subgenus of synthetic or natural compounds set forth in claim 17, we find the appellants' reliance on the antibodies and antibody fragments disclosed in the specification to be misplaced. Brief, p. 14. We point out that antibodies and fragments thereof are proteins; a group of compounds which claim 17 explicitly states is excluded from the subgenus of synthetic and natural compounds set forth therein. Moreover, even if we consider the entire specification, we find no disclosure of any synthetic or natural compounds which will perform in the claimed method. Accordingly, we agree with the examiner that the specification fails to provide an adequate written description of the method set forth in claim 17.[2] See, University of

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[2] Even if we assume, arguendo, that the appellants intended to argue that the disclosure of computer-assisted drug design set forth on pages 26-27 of the specification, provides written descriptive support for synthetic or natural compounds capable of performing in the method described in claim 17, we would find said disclosure to be insufficient. We point out that the specification simply states :

> [c]omputer modeling technology allows visualization of the three-dimensional atomic structure of a selected molecule and the rational design of new compounds that will interact with the molecule. . . . The computer graphics systems enable prediction of how a new compound will link to the target molecule and allow experimental manipulation of the structures of the compound and target molecule to perfect binding specificity. Prediction of what the molecule-compound interaction will be when small changes are made in one or both requires molecular software and computationally intensive computers, usually coupled with user-friendly, menu-driven interfaces between the molecular design program and the user.

California v. Eli Lilly and Co., 119 F.3d at 1559, 43 USPQ2d at 1406 ("[N]aming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material").

With respect to oligonucleotides capable of binding to the EPCR as set forth in claim 27, we find that the specification states that

> [m]ethods to produce or synthesize oligonucleotides are well known in the art. . . DNA sequences of the 5' flanking region of the receptor protein gene described herein can be used to design and construct oligonucleotides including a DNA sequence consisting essentially of at least 15 consecutive nucleotides with or without base modifications or intercalating agent derivatives, for use in forming triple helices specifically within the 5' flanking region of a receptor protein gene in order to inhibit expression of the gene. Specification, p. 31, lines 11-31.

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* * *

> Although described above with reference to design and generation of compounds which could alter binding, one could also screen libraries of known compounds, including natural products or synthetic chemicals, and biologically active materials, including proteins, for compounds which are inhibitors or activators.

From the foregoing, we find that the specification only provides a research plan to obtain a yet-to-be-discovered compound. Since the specification does not describe any natural or synthetic compounds, which are not proteins, peptides or nucleic acid sequences, having the functional characteristic of binding to the EPCR in an amount which blocks the binding of protein C or activated protein C, we find that it fails to provide an adequate written description of the method set forth in claim 17. That is to say, since the specification fails to reasonably convey that the appellants were in possession of a natural or synthetic compound to perform the claimed method, it reasonably follows that we find that they were not in possession of said method at the time the application was filed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1555, 19 USPQ2d at 1116.

Here, we agree with the examiner that only oligonucleotides described in the specification which inhibit EPCR expression are antisense sequences which are complementary with, and therefore "bind" (hybridize) to the EPCR nucleotide sequence. We do not find, and the appellants have not pointed out, any teachings in the specification of an oligonucleotide which binds to the EPCR as set forth in claim 27. Nor do we find, and the appellants have not provided, any evidence that one skilled in the art would have understood that there is a structure-function relationship between the amino acid sequence of the receptor and an oligonucleotide which can bind thereto. Thus, we find that the appellants have only described the oligonucleotides recited in the claim by their function. As discussed above, the Federal Circuit has held that for a nucleotide sequence, an adequate written description "requires a precise definition" which is "sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d at 1566, 43 USPQ2d at 1405, quoting, Fiers v. Revel, 984 F.2d at 1171, 25 USPQ2d at 1606. Since the specification does not provide such a definition, we find that it fails reasonably to convey to those skilled in the art that the appellants were in possession of the method set forth in claim 27 at the time the application was filed. Vas-Cath Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

Contrary to the appellants' argument, we do not find that the specification describes any fragments of the EPCR which are capable of binding thereto in the

manner required by claim 28. Rather, we find that the specification discloses general techniques for preparing soluble fragments of the EPCR to use (i) to block binding of the receptor in general; and (ii) as antigens to generate antibodies. See, the specification, pages 32-33. However, with respect to subsection (i), we find that the specification does not indicate whether the receptor fragments block binding of the EPCR by binding to the EPCR itself, or by binding to ligands such as protein C and activated protein C which recognize the receptor. We point out that receptor fragments that bind to protein C or activated protein C are not within the scope of the claimed method. That is, the claims are directed only to those compounds which bind to the EPCR and not to the ligands protein C and activated protein C. In any event, we find that the specification fails to describe any receptor fragments that will perform the method described in claim 28, and there is no evidence that such compounds are known in the art. Accordingly, we find that the specification fails to reasonably convey to those skilled in the art that the appellants were in possession of said method.

As to the appellants' arguments concerning claims 29 and 30, we point out that since we find that the specification fails to provide an adequate written description of the genus described in the base claim 16, from which these claims depend, it reasonably follows that our analysis with respect to claim 16 also applies to the subject matter of these claims.

II. Enablement

The examiner also argues that the claims fail to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. Answer, p. 7. However, in view of our affirmance of the rejection on the written description ground, the enablement rejection is moot. Accordingly, we need not discuss it further.

New Ground of Rejection

Under the provisions of 37 C.F.R. § 41.50(b), we enter the following new ground of rejection:

Claim 26 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It appears that the examiner inadvertently omitted claim 26 from the rejection of the claims discussed above. We point out the claim 26 is dependent on claim 16. Thus, it reasonably follows that our findings with respect to the failure of the specification to provide an adequate written description of the genus of compounds capable of binding to an endothelial cell protein C/activated protein C receptor in the manner set forth in claim 16, is equally applicable to the claim 26 wherein said compounds are said to be labeled.

In view of the foregoing the decision of the examiner is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. 1.136(a).

AFFIRMED; NEW GROUND OF REJECTION

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